IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	Heger et al.	Docket No.:	49619
Serial No.:	09/857,480	Confirmation No.:	4809
Filing Date:	8/13/2002	Examiner:	YOUNG, MICAH PAUL
Customer No.:	26474	Art Unit:	1618

For: Nanoparticulate core shell systems and the use thereof in pharmaceutical and cosmetic preparation

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants request review of the final rejection in the above-identified application. No amendments are being filed with this request. This request is being filed with a notice of appeal. The review is requested for the reasons stated on the attached sheets.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees, to Deposit Account 14.1437. Please credit any excess fees to such account.

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Status of Claims 2

Arguments 2

Status of Claims: Claims 15 – 21 and 23 – 27 are pending. Claims 15 – 21 and 23 – 27 stand rejected.

Arguments:

In the final Office Action of June 22, 2007, the Examiner rejected:

I. Claims 15 – 18 and 23 – 27 under 35 U.S.C. §103(a) over *Vallet Mas et al.* (EP 0 717 989) in view of *Redlich et al.* (US 5,225,279),

II. Claims 19 and 20 under under 35 U.S.C. §103(a) over *Vallet Mas et al.* in view of *Weitshies et al.* (US 6,068,857), and

III. Claim 21 under 35 U.S.C. §103(a) over *Vallet Mas et al.* in view of *Liversidge et al.* (US 6,045,829).

Regarding Rejection I:

The rejection of claims 15 – 18 and 23 – 27 under 35 U.S.C. §103(a) over *Vallet Mas et al.* (EP 0 717 989) in view of *Redlich et al.* (US 5,225,279) is in clear error.

The process of claim 15, and the process by which the product of claim 26 is produced, comprise mixing an active ingredient/polymer solution or precipitate with an aqueous solution of a polymeric coating material. The specification explains that "[i]n one embodiment of the process, a molecularly disperse solution of the active ingredient in the chosen solvent is prepared together with the polymer which is to be present in the active ingredient preparation in the core of the particles."[1] According to independent claims 15 and 26, the active ingredient is an X-ray amorphous active ingredient, and the polymer in the active ingredient/polymer solution is one or more copolymers of acrylates, methacrylates, methacrylic acid or acrylic acid.

The combination of references, proposed by the Examiner, fails to teach or suggest the utilization of an active ingredient that is an X-ray amorphous active ingredient. The Examiner acknowledges that neither reference requires an X-ray

[1] Page 7, lines 43 – 46, the specification.

amorphous active ingredient. Yet the Examiner takes the position that "the drug [utilized in the *Vallet Mas et al.* reference] is amorphous or at least non crystalline in nature since dissolution is not required, and the core emulsion solution is not a suspension of materials." This argument is improper. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'"[2] A person of ordinary skill in the art would not conclude that the active ingredient utilized in the *Vallet Mas et al.* reference is necessarily an X-ray amorphous active ingredient on the basis posited by the Examiner. For this reason, the combination of references cited in this rejection fails to establish a *prima facie* case of obviousness.

The combination of references, proposed by the Examiner, also fails to teach or suggest mixing an active ingredient/polymer solution or precipitate with an aqueous solution of a polymeric coating material, wherein the polymer in the active ingredient/polymer solution is one or more copolymers of acrylates, methacrylates, methacrylic acid or acrylic acid. However, the Examiner argues that "[t]he '279 patent discloses core/shell particles comprising acrylate and methacrylate copolymers .... [and that, therefore, a] skilled artisan would be motivated to include the methacrylate polymers in order to incorporate water-insoluble active agents such as isothiazolenoe."[3] The Examiner's argument is based on an over-simplification of the cited references. When the references are considered for what they would have disclosed to a person of ordinary skill in the art at the time the claimed invention was made, it becomes clear that no "apparent reason to combine known elements in the fashion claimed"[4] existed, and that the Examiner's proposed combination would actually change the principle of operation of the inventions being modified.

The invention according to *Redlich et al.*, "provides an improved process for producing aqueous dispersions of polymeric core/shell particles prepared by sequential

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[2] MPEP § 2112, citing In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).
[3] Page 3, lines 12 – 17 of the present Office action.
[4] *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ___ (2007), Slip op. at 14, 127 S.Ct. 1727 at 1741.

microsuspension polymerization having a core containing a solvent blend."[5] The process of *Redlich et al.* comprises:

(a) preparing a core emulsion containing an initial monomer,

(b) heating the core emulsion to polymerize the initial monomer, thereby forming core particles,

(c) adding at least one base, and

(d) optionally adding additional monomer which is polymerized on the core/shell particles.

Thus, despite the Examiner's oversimplification of the *Redlich et al.* reference to a mere disclosure of "core/shell particles comprising acrylate and methacrylate copolymers[,]"[6] a person of ordinary skill in the art would understand that in the *Redlich et al.* process, core/shell particles are prepared by sequential microsuspension polymerization.

On the other hand, the process disclosed in the *Vallet Mas et al.* reference involves mixing two "phases continuously while maintaining constant the relationship between the phases and the mixture volume and simultaneously spraying the resultant mixture in an evaporation system with temperature and vacuum conditions which provide for the instantaneous evaporation of the solvent from the polymer causing the deposition of the polymer around the particles or droplets."[7]

It should be clear that the Examiner's proposed combination involves not mere modification of, but complete abandonment of the principle of operation (sequential microsuspension polymerization) of the *Redlich et al.* process. Of course, "[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious."[8] For this reason, in addition to the reasons discussed above, the combination of references cited in this rejection fails to establish, a *prima facie* case of obviousness.

Indeed, a skilled artisan had no apparent reason to oversimplify the *Redlich et al.* reference to a mere disclosure of "core/shell particles comprising acrylate and

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[5] Column 4, lines 44 – 48 of US 5,225,279.
[6] Page 3, lines 12 – 13 of the present Office action.
[7] Abstract EP 0 717 989 A1.
[8] MPEP §2143.01, citing In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

methacrylate copolymers[,]"[9] no apparent reason to abandon the principle of operation (sequential microsuspension polymerization) of the *Redlich et al.* process, and no apparent reason to make the combination/modification proposed by the Examiner. Thus, a *prima facie* case of obviousness has not been established.

Regarding Rejections II and III:

The rejection of claims 19 and 20 under under 35 U.S.C. §103(a) over *Vallet Mas et al.* in view of *Weitshies et al.* (US 6,068,857), and the rejection of claims 21 under 35 U.S.C. §103(a) over *Vallet Mas et al.* in view of *Liversidge et al.* (US 6,045,829) are in clear error.

Claims 19 and 20 and 21 depend from claim 15. The combinations of references, proposed by the Examiner, fail to teach or suggest mixing an active ingredient/polymer solution or precipitate with an aqueous solution of a polymeric coating material, wherein the polymer in the active ingredient/polymer solution is one or more copolymers of acrylates, methacrylates, methacrylic acid or acrylic acid. The Examiner has made no attempt to compensate for this shortcoming in either reference. Thus, a *prima facie* case of obviousness has not been established.

Additionally, this combination of references fails to teach or suggest the utilization of an active ingredient that is an X-ray amorphous active ingredient. As discussed regarding the previous rejection, a person of ordinary skill in the art would not conclude that the active ingredient utilized in the *Vallet Mas et al.* reference is necessarily an X-ray amorphous active ingredient on the basis posited by the Examiner. For this reason, the combination of references cited in this rejection fails to teach or suggest all of the claim limitations. Thus, a *prima facie* case of obviousness has not been established.

Regarding the showing of unexpected results:

Since a *prima facie* case of obviousness has not been established a showing of unexpected results is in no way required, however, as expressed in the specification,

[9] Page 3, lines 12 – 13 of the present Office action.

"Surprisingly, the colloidal active ingredient preparations according to the invention show distinctly less growth of hydrosol particles than known active ingredient preparations which consist essentially exclusively of active ingredient mass in the core of the colloidal particles One hour after the aqueous hydrosols have been prepared in the presence of a solvent dissolving the active ingredient, the particle growth is a factor of 4 to 10 less In the case of aqueous hydrosols which contain no solvent dissolving the active ingredient, the particle growth is reduced by a factor of 1.5 - 5."[10]

In Conclusion:

The rejections are based on clear errors. Little, if any, interpretation of the claims or the references is required to conclude that the rejections should be withdrawn. The present application is in condition for allowance. Favorable action is respectfully requested. In order to facilitate the resolution of any issues or questions presented by this paper, please feel free to contact the undersigned by phone to further the discussion.

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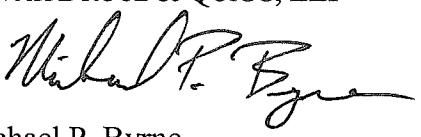

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[10] Page 3, indicated lines 30 – 39 of the present Specification.